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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/742,512	12/20/2000	Jean-Christophe Audonnet	454313-2541.2	8436

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EXAMINER	
FORD, VANESSA L	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 02/07/2003 14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/742,512	Applicant(s) AUDONNET ET AL.	
	Examiner Vanessa L. Ford	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-56* is/are pending in the application.

4a) Of the above claim(s) *4-17,19,20,22,23,26-29,32,33,37-44 and 46-55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,18,21,24,25,30,31,34-36,45 and 56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4)☒ Interview Summary (PTO-413) Paper No(s). *13* .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

1. Applicant's response to the Restriction requirement filed on November 7, 2001 is acknowledged. Applicant's election of without traverse, claims Group I, claims 1-36 and 45, species bovine and presentation of the composition in antigen form (i.e. vectors not elected) is acknowledged. Claim 1 has been amended and claim 56 has been added. Claims 37-44 and 46-56 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being to a non-elected invention. Claims 4-17, 19-23, 26-29 and 32-33 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being to a non-elected species. Claims 1-3, 18, 21, 24-25, 30-31, 34-36, 45 and 56 are under examination.

Specification Objections

2. The specification has been objected to because of the use of trademarks on page 22 in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

3. The specification is objected to because of the use of the term "Combo" and "Crypto" on page 40. The proper terms "combination" and "*Cryptosporidium*" should be used. Correction is required.

4. The specification is objected to because of the recitation "The invention shall now be further described by the following numbered paragraphs" (pages 43-48). These "paragraphs" appear to be the same as the claims on pages 53-57 of the specification. Claims should be designated as claims and not paragraphs. Clarification is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-3, 18, 21, 24-25, 30-31, 34-36, 45 and 56 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a vaccine comprising a P21 antigen and a Cp15/16 antigen does not reasonably provide enablement for a vaccine comprising epitopes of a P21 antigen and epitopes of a Cp15/16 antigen.

The claims are drawn to a combination immunological, immunogenic or vaccine composition comprising a first antigen or epitope of interest from a first enteric pathogen comprising *Cryptosporidium* and/or a first vector that expresses the first antigen or epitope of interest, and a second antigen or epitope of interest from a second enteric pathogen and/or the first vector that expresses the first antigen or epitope of interest also expresses the second antigen or epitope of interest and a pharmaceutically acceptable vehicle when the first and second enteric pathogens can be the same

enteric pathogen or different enteric pathogens and a kit comprising the combination composition and optionally comprising instructions for admixtures and/or administration.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The specification teaches that P21 (page 14) and Cp15/16 (page 14) are to be included in the claimed immunogenic composition or vaccine. The specification is enabling only for the claims limited to the P21 antigen and the Cp15/16 antigen as disclosed in the specification. The specification is not enabling for the epitopes of P21 and Cp15/16. The specification mentions that polypeptides which can be used in the practice of the instant invention have at least 75% homology or identity to the P21 antigen or the Cp15/16 antigen (pages 15-16). The specification states that one skilled in the art could make and use polypeptides that are at least 75% homologous or identical to the P21 and Cp15/16 antigen. The specification does not disclose <u>any specific</u> structural information about the epitopes or fragments of the P21 or Cp15/16 antigens. The specification does not disclose, What amino acids are involved in these epitopes or fragments? What amino acid substitutions or deletions can be made in the polypeptide so that the polypeptide retains the same activity as the P21 and Cp15/16 antigens? One skilled in the art would require guidance in order to make or use the epitopes or fragments of the above recited *Cryptosporidium parvum* antigens in a manner reasonable in correlation within the scope of the claims.

Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification regarding how to make and use epitopes or fragments of the P21 and Cp15/16 antigen, and 3) the relative skill of those in the art is commonly recognized as quite high (post - doctoral level).

In view of all of the above, it is determined that it would require undue experimentation to make and use epitopes or fragments of the P21 and Cp15/16 antigens in commensurate in scope with the claims. Because of lack of guidance provided in the specification, it is determined that the specification is not enabled for an immunogenic composition or vaccine that comprises epitopes or fragments of the P21 and Cp15/16 antigens.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 45 recites the term "optionally". It is unclear as to what the applicant is referring? Are the instructions included in the kit? Clarification is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1-3, 18, 21, 24-25, 30-31, 34-36, 45 and 56 are rejected under 35 U.S.C. 103(a) as unpatentable over Perryman et al *(WO 98/07320, published February 26, 1998)* in view of Jenkins et al (*U.S. Patent No. 5,591, 434, published January 7, 1997).*

Claims 1-3, 18, 21, 24-25, 30-31, 34-36, 45 and 56 are drawn to a combination immunological, immunogenic or vaccine composition comprising a first antigen or epitope of interest from a first enteric pathogen comprising *Cryptosporidium* and/or a first vector that expresses the first antigen or epitope of interest, and a second antigen or epitope of interest from a second enteric pathogen and/or the first vector that expresses the first antigen or epitope of interest also expresses the second antigen or epitope of interest and a pharmaceutically acceptable vehicle when the first and second

enteric pathogens can be the same enteric pathogen or different enteric pathogens and a kit comprising the combination composition and optionally comprising instructions for admixtures and/or administration.

Perryman et al teach a vaccine formulation that comprises recombinant C7 protein from *Cryptosporidium parvum* (SEQ ID NO: 12, which is P21) in monophosphoryl lipid A trehalose dimycolate adjuvant (pages 25-26). Perryman et al teach the use of recombinant proteins and synthetic peptides containing *Cryptosporidium parvum* epitopes for inducing an antigenic response in animals (see the Abstract). Perryman et al teach that the vaccine formulations comprising the antigens of the invention can be prepared for both human and veterinary treatments. Perryman et al teach that the vaccine formulations comprise appropriate antigen and a pharmaceutically acceptable carrier (page 11). Perryman et al also teach that the vaccine formulations of the invention may comprise a suitable adjuvant such as aluminum hydroxide or aluminum phosphate and further comprise stabilizers such as carbohydrates or glucose (page 12). Perryman et al teach that the vaccine formulations may include combinations of appropriate antigens (page 11).

Perryman et al do not teach the use of the Cp15/16 antigen of *Crytosporidium parvum.*

Jenkins et al teach the use of Cp15/16 recombinant proteins which are effective in the immunization of animals against cryptosporidiosis (columns 2, lines 6-9). Jenkins et al teach that Cp15/16 proteins are preferred in the treatment of bovine and are administered in the presence of a physiologically acceptable diluent (column 7, lines 59-

67). Jenkins et al teach that the Cp15/16 protein compositions may also include vaccine stabilizers and adjuvants (column 8, lines 1-8). It is well known in the art to package each antigen used in the claimed invention in separate containers, package them together in a kit which includes instructions for preparing admixtures and instructions for administering the claimed composition.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to add the Cp15/16 vaccine composition of Jenkins et al to the vaccine formulations of Perryman et al because Perryman et al teach that the vaccine formulations may include combinations of appropriate antigens (page 11). It would be expected barring evidence to the contrary that a vaccine comprising both the P21 antigen and the Cp15/16 antigen would be effective against cryptosporidiosis because Jenkins et al teach that Cp15/16 proteins are effective for immunization of a variety of animals against *Cryptosporidium parvum*, particularly for the production of hyperimmune colostrums that may be used to confer passive immunity against the parasite in young or immunodeficient animals (column 8, lines 14-22) and Perryman et al demonstrates that immunization of adult cows with P21 gave high titers of antibodies to the P21 antigen and to the native P23 antigen (page 26). Perryman et al also demonstrated that colostrums collected from immunized cows also gave high titers of antibodies to P21 and the native P23 (page 26) and Perryman et al suggest that the antibodies may impart passive immunity to *Cryptosporidium parvum* in an animal subject in need thereof (page 11).

Pertinent Prior Art

8. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure *(Perryman et al, U.S. Patent No. 6,323,020, published November 2001).*

Status of Claims

9. No claims are allowed.

Conclusion

10. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (703) 308-4735. The examiner can normally be reached on Monday – Friday from 7:30 AM to 4:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308–3909.

Vanessa L. Ford
Biotechnology Patent Examiner
January 31, 2003

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